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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/803,778	03/12/2001	Bridget Kathleen Mapleson	1324.024A	9665

23405 7590 02/18/2004

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ALBANY, NY 12203

EXAMINER

ZEMAN, ROBERT A

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 02/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/803,778

Applicant(s)

MAPLESON ET AL.

Examiner

Robert A. Zeman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 November 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 and 7-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7-12 and 14-20 is/are rejected.
- 7) ☒ Claim(s) 13 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11-10-2003 has been entered.

The amendment and response filed on 11-10-2003 are acknowledged. Claims 1-5 have been amended. Claims 1-5 and 7-20 are pending and currently under examination.

Claim Rejections Withdrawn

The rejection of claims 1-4 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "vaccine substance" is withdrawn in light of the amendment thereto.

The rejection of claim 4 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the term "vaccine antigen" is withdrawn in light of the amendment thereto.

Claim Rejections Maintained

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7-12 and 14-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shanbrom (EP 0 083 999) in view of Shanbrom (U.S. Patent 4,315,919) for the reasons set forth in the previous Office action in the rejection of claims 1-5 and 7-20.

Applicant argues:

1. Shanbrom ('919) while suggesting the use of any amphiphilic surfactant, including ionic and non-ionic surfactants, provides working examples using a non-ionic surfactant (Triton-X 100) and includes a protein precipitation step.
2. Shanbrom ('919) contains a disclaimer with respect to the use of ionic surfactants such as deoxycholate. Said disclaimer is in agreement with applicant's statement that deoxycholate could not be used on large-scale vaccine preparations.
3. Shanbrom ('919) discloses but does not demonstrate that ionic amphiphiles are effective in removing endotoxin when used in conjunction with protein precipitation methods to destroy the

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endotoxin prior to their separation and removal along with the amphiphile in the supernatant (col. 4, lines 20-29).

4. Shanbrom (EP) teaches treatment of a variety of substances including a non-proteinaceous polysaccharide vaccine, heparin and dehydrostreptomycin sulfate using the non-ionic surfactant Triton-X 100 followed by precipitation with polyethylene glycol.

5. Given the disclaimer in Shanbrom ('919) regarding ionic surfactants one of skill in the art would not be motivated to combine the cited references. Thus it would not be obvious for one of ordinary skill, based on the cited references, to use an ionic surfactant to remove pyrogen from an amphiphilic drug or vaccine then filter the solution to remove the ionic surfactant without an additional precipitation step (as suggested by Shanbrom '919).

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Points 1 and 5: As outlined previously Shanbrom (EP 0 083 999) discloses a method of purifying biological, pharmaceutical and biomedical products comprising contacting said product with a **non-denaturing surfactant** (see pages 5-7). This encompasses **ionic** surfactants. Shanbrom further discloses the use of ultrafiltration techniques (including dialysis) to separate the biomedical product from surfactant and dissociated impurities (see page 10).

Shanbrom discloses that his method can be used for purifying both **proteinaceous** (see page 5) and non-**proteinaceous** (see page 7) products. Shanbrom differs from the claimed invention in that he does not explicitly disclose the use of ionic surfactants such as deoxycholate or the use of filters comprising regenerated cellulose acetate membrane or a polysulfone membrane.

Shanbrom (U.S. Patent 4,315,919) disclose a method of removing pyrogens (endotoxins) from

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biological and biomedical products utilizing a myriad of surfactants (see columns 1-5). Said surfactants include cationic, anionic, ampholytic and nonionic surfactants (see column 1, line 48 to column 2, line 50) Said surfactants also include salts of bile acids including sodium deoxycholate. Shanbrom further discloses that it might be necessary to separate the purified product from the surfactant and impurities (see column 3, line 67 to column 4, line 2). Consequently, it would have been obvious to one of ordinary skill in the art to utilize the various surfactants disclosed by Shanbrom (U.S. Patent 4,315,919) in the methods disclosed by Shanbrom (EP 0 083 999) since Shanbrom (EP 0 083 999) discloses the use of all non-denaturing surfactants (see page 5, lines 13-14) and Shanbrom (U.S. Patent 4,315,919) merely lists various non-denaturing surfactants. It should be noted that neither Shanbrom reference explicitly disclose the use of filters comprising regenerated cellulose acetate membrane or a polysulfone membrane. However, Shanbrom (EP 0 083 999) disclose the parameters to be used in his ultrafiltration techniques and hence, the use of a regenerated cellulose acetate membrane or a polysulfone membrane constitutes obvious variants of the disclosed ultrafiltration technique. Finally, the surfactant concentrations recited in claims 14-16 are equally obvious since one of ordinary skill in the art would optimize disclosed methods.

With regard to Points 2-3: While Applicant is correct that Shanbrom '919 discloses that the use of deoxycholate as the surfactant requires an additional precipitation step due to the reversibility of the endotoxin disassociation, said "disclaimer" relates to deoxycholate specifically, not ionic surfactants generally. Hence the cited references to render obvious any claims (i.e. claim 13) are limited to the use of deoxycholate as the amphiphilic surfactant used.

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With regard to Point 4, the basic method disclosed in Shanbrom (EP) does not include a precipitation step (see page 6, line 5-35 and example 1).

Claim Objections

Claim 1 is objected to because of the following informalities: Said claim contains an obvious typographical error. The word "thereafer" should read "thereafter". Appropriate correction is required.

Conclusion

No claim is allowed.

Claims 1-5, 7-12 and 14-20 are rejected.

Claim 13 is objected to as being dependent on a rejected claim.

Claim 13 is free of the art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866.

The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert A. Zeman
February 12, 2004


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